

## **REMARKS**

Claims 1-4, 8, 16, 19 and 20 were pending in the instant application. Applicants have cancelled claim 8 in view of new claims 93-109, which present the subject matter of the canceled claim. Applicants have also cancelled claims 2 and 9-92 without prejudice and reserve the right to pursue the subject matter of the cancelled claims in one or more related applications. Applicants have amended pending claims 1 and 3 and have added new claims 93-120 for clarity and to more specifically point out and distinctly claim the invention. Applicants have further amended withdrawn claims 5-7 for consistency with the amendments to the currently pending claims in the event of rejoinder. Support for the amendments and new claims may be found throughout the specification, for example, support for the amendments to claims 1 and 3-7 may be found, *inter alia*, in paragraph [0033] at page 13, [0060] at page 22, [0093] at page 31, and [00108] at page 38; and support for new claims 93-120 may be found at paragraph [0013]- [0015] at pages 6-7, [0017] at page 8, [0018] at page 8, [0032] at page 13, [0035] at pages 13-14, [0036] at page 14, [0040] at pages 14-15, [0041] at page 15, [0043]-[0047] at pages 15-16, [0048] at page 16, [0053] at page 18, [0055] at page 18, [0057] at page 19, and [0093] at pages 31-32. Accordingly, no new matter has been introduced. After entry of this amendment, claims 1, 3-4, and 93-116 will be pending.

### **Objections to the Claims**

The Examiner has objected to claim 20 because of alleged editorial informalities. Applicants have canceled claim 20, rendering the instant objection moot and therefore request that the objection to the claims be withdrawn.

### **Provisional Rejection For Obviousness-Type Double Patenting**

Claims 1-4, 8, 16, 19 and 20 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 8 of U.S. Patent No. 6,787,318 ("the '318 application"). The Examiner contends that the claims are not patentably distinct from each other because claim 8 of the '318 application allegedly embraces all limitations of the instant claims and, therefore, anticipates the instant claims. Claims 1-4, 8 and 19 are further provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 4, 5, 11 and 12 of U.S. Patent Application Serial No. 11/523,468 ("the '468 application"). The examiner

contends that the claims are not patentably distinct because the instant claims allegedly encompass the claims of the '468 application.

In response, and without agreeing with the rejection, Applicants request that the obvious-type double patenting rejections be held in abeyance until indication of allowable subject matter.

*The rejections under 35 U.S.C. § 112, second paragraph, should be withdrawn*

The Examiner has objected to claim 1 under 35 U.S.C. § 112, Second Paragraph, as allegedly indefinite. In particular, the Examiner alleges that it is unclear whether the marker for the cells contacted with the CD40 ligand is the same as that for the cells contacted with the CD40 ligand and the compound (*i.e.*, it is unclear whether the marker is the same in steps (i) and (ii) of claim 1 as amended herein). In response, Applicants have amended claim 1, in part, to recite in step (ii) (as amended herein) that "said one or more markers" is measured. Applicants submit that the amendment obviates or overcomes the instant rejection both with respect to claim 1 as well as with respect to the claims dependent or ultimately dependent thereon, *i.e.*, claims 3-4 and new claims 93-120.

The Examiner has further rejected claim 1 under 35 U.S.C. § 112, Second Paragraph, as allegedly indefinite for failing to include an essential step. In particular, the Examiner contends that a necessary step of the method of claim 1 is a step reciting that the comparison between the first and second sample leads to the identification of a compound that modulates the CD40L/CD40R signaling pathway. In response, Applicants have amended claim 1 in accordance with the Examiner's suggestion. Applicants have amended claim 1, in part, to include the text, "wherein a difference in the levels or amounts of the said one or more markers measured in steps (i) and (ii) indicates a compound that modulates the CD40L/CD40R signaling pathway." Applicants submit that the amendment obviates or overcomes the instant rejection both with respect to claim 1 as well as with respect to the claims dependent or ultimately dependent thereon, *i.e.*, claims 3-4 and new claims 93-120.

The Examiner has also rejected claims 2-4, 8, 16, 19 and 20 under 35 U.S.C. § 112, Second Paragraph, as indefinite for reciting "the method of claim 1" wherein allegedly no antecedent basis for the limitation exists in claim 1. As discussed above, claims 2, 8, 16, 19 and 20 have been canceled. With respect to the pending claims, applicants have amended claim 1, in part, such that it is now drawn to a method for screening compounds. Applicants submit that the amendment obviates or overcomes the instant rejection both with respect to currently pending claims 3-4 as well as with respect to new claims 93-120.

The Examiner has also rejected claims 2, 8 and 16 under 35 U.S.C. § 112, Second Paragraph, as indefinite because each claim allegedly recites both broad and narrow ranges or limitations. As discussed, Applicants have canceled claims 2 and 16. With respect to claim 8, Applicants have canceled claim 8 in favor of new claims 93-109. Applicants believe that the separation of groups of compounds originally recited in claim 8 into separate claims as well as the introduction of dependent claims within the separate “groups” of compounds addresses the Examiner’s concerns. Accordingly, Applicants submit that the amendments to the claims obviate or overcome the instant rejection both with respect to claim 8 and with respect to new claims 93-109.

The Examiner further rejects claim 1 under 35 U.S.C. § 112, Second Paragraph, as allegedly indefinite in that it is drawn to a research model but recites method steps. In response, as discussed, Applicants have amended claim 1, in part, such that is now drawn to a screening method for compounds that modulate the CD40L/CD40R signaling pathway. Applicants believe that amendment obviates or overcomes the instant rejection with respect to claim 1 and with respect to claims dependent or ultimately dependent thereon, *i.e.*, claims 3-4, and 93-120.

The Examiner has rejected claims 1-4, 8, and 19 under 35 U.S.C. § 112, Second Paragraph, as indefinite for allegedly omitting an essential element. In particular, the Examiner contends that the screening method requires that the cells express CD40R and that the claims do not recite this limitation. Applicants point out that claims 2, 8 and 19 have been canceled. With respect to the pending claims, applicants have amended claim 1, in part, to recite that the cells used in the screening method express CD40R. Applicants submit that the amendment obviates or overcomes the instant rejection with respect to claim 1 and to claims dependent or ultimately dependent thereof, *i.e.*, claims 3-4 and claims 93-120.

In view of the foregoing, Applicant requests the rejections under 35 U.S.C. § 112, Second Paragraph, be withdrawn.

*The rejections under 35 U.S.C. § 102 (b) should be withdrawn*

The Examiner has rejected claims 1-4 under 35 U.S.C. § 102(b) as allegedly anticipated by Tan et al., 1999, Science 286:2352-2355 (“Tan”). In response, although not agreeing with the Examiner’s contention and merely to advance prosecution, Applicants have amended claim 1, in part, such that is now drawn to an *in vitro* method of screening for compounds that modulate the CD40L/CD40R signaling pathway comprising contacting neuronal cells that express CD40R with CD40L in the presence or absence of said compound.

Tan teaches screening methods using animal models and cultures of primary microglial cells isolated from said animal models, but does not teach or describe the use of an *in vitro* system comprising neuronal cells as instantly claimed. Accordingly, Tan does not teach or describe each and every element of claim 1 as amended herein, and, thus, cannot anticipate claim 1. Because Tan does not anticipate claim 1, it does not anticipate claims 3-4 and 93-120 as dependent or ultimately dependent thereon.

The Examiner further rejects claim 1 under 35 U.S.C. § 102(b) as allegedly anticipated by Force et al., U.S. Patent Application Publication No. 2003/0059427 ("Force"). Tan et al., 1999, Science 286:2352-2355 ("Tan"). Applicants respectfully disagree with the Examiner's position.

Force teaches generally the isolation and characterization of an anti-CD40R antibody and specifically demonstrates the activity of the antibody in an assay of B cell proliferation, wherein the B cells are derived from primary tonsillar cultures. However, Force neither teaches or describes the use of neuronal cells in an *in vitro* method of screening for compounds that modulate the CD40L/CD40R signaling pathway as required by claim 1 as amended herein. Accordingly, Force does not teach or describe each and every element of claim 1, and, thus, cannot anticipate claim 1. Because Force does not anticipate claim 1, it also does not anticipate claims 3-4 and 93-120 as dependent or ultimately dependent thereon.

In view of the foregoing, Applicant submits that the instant rejections have been obviated or overcome and request that the rejections under 35 U.S.C. § 102(b) be withdrawn.

*The rejections under 35 U.S.C. § 103 should be withdrawn*

*The rejection over Tan in view of Zheng and Gerritse*

The Examiner has rejected claims 1-4, 8, 16, 19 and 20 under 35 U.S.C. § 103 as allegedly obvious over Tan in view of Zheng et al., U.S. Patent Application Publication No.: 2004/0067982 ("Zheng") and Gerritse et al., 1996, P.N.A.S. USA 93:2499-2504 ("Gerritse"). Applicants point out that claims 2, 8, 16, 19 and 20 have been canceled. With respect to the pending claims, Applicants respectfully disagree with the Examiner's position for the following reasons.

As discussed above, Tan teaches and describes the use of animal models and/or primary microglial cells derived from the animal models for evaluating compounds that affect CD40L/CD40R interaction. Tan is particularly directed to the characterization of microglial cell activation as the mediator of the disease state and offers no suggestion or motivation that a compound of interest could be effectively evaluated in a system based on neuronal cells that express CD40. Thus, Tan does not render obvious the invention as instantly claimed.

Zheng does not remedy the deficiencies of Tan. Zheng presents methods of manufacture and characterization of compounds that bind CD40L. Zheng stresses the role of CD40R and CD40L in immune cell activity (particularly B and T cell activity), but does not teach or suggest that CD40 is even present on neuronal cells, much less that modulation of CD40L/CD40R interaction results in a detectable activity in cultures of neuronal cells. Moreover, Zheng provides only cell-free assays for evaluating whether a compound interferes with the direct binding of CD40L to CD40R and, thus, cannot suggest or provide motivation for a cell-based assay that evaluates the response of a cellular marker as a result of the modulation of the CD40L/CD40R interaction. Accordingly, Zheng, whether alone or in combination with Tan fails to render obvious the instantly claimed invention drawn, in part, to a method of screening compounds that modulate the signaling pathway of CD40R/CD40L comprising the use of neuronal cells.

Similarly, Gerritse fails to remedy the deficiencies of Tan, whether alone or in combination with Zheng. Gerritse provides an *in vivo* system for evaluation of the effects of CD40L antibody on an animal model of experimental allergic encephalomyelitis (“EAE”). Gerritse describes the CD40R/CD40L interaction as primarily a mediator of immune cell function, particularly, cells of monocytic origin, and concludes that the effects of the anti-CD40L antibody were mediated via regulation of immune cell function within the central nervous system, *i.e.*, regulation of B cells, T cells and/or microglia,. Thus, like Tan, Gerritse cannot render obvious a screening system based on the activity of cell that is not an immune cell, *e.g.*, a neuronal cell that expresses CD40R as instantly claimed in claim 1. Accordingly, Gerritse, whether alone or in combination with Tan and/or Zheng fails to render obvious the instant invention as claimed in claim 1 or in claims 3-4 and 93-120 as dependent thereon.

*The rejection over Force in view of Zheng and Gerritse*

The Examiner has further rejected claims 1, 8, 16, and 19 under 35 U.S.C. § 103 as allegedly obvious over Force in view of Zheng and Gerritse. Applicants point out that claims 8, 16, and 19 have been canceled. With respect to the pending claims, Applicants respectfully disagree with the Examiner’s position for the following reasons.

As described above, Force provides for the isolation and characterization of an anti-CD40R antibody using assay of B cell proliferation. Force provides no suggestion or motivation that such an assay would be effective in a system not based on the activity of a B-cell, *i.e.*, based on the activity of neuronal cells that express CD40. Therefore, Force cannot render obvious a screening method comprising neuronal cells as instantly claimed.

Neither Zheng nor Gerritse remedy the deficiencies of Force. As discussed above, neither of these references provides suggestion or motivation that a screening assay would be

effective where the assay is not dependent on the activity of a cell of the immune system, e.g., a system based on the activity of neuronal cells expressing CD40R as instantly claimed. Accordingly, Zheng or Gerritse, whether alone or in combination with Tan, and/or Zheng fails to render obvious the instant invention as claimed in claim 1 or in claims 3-4 and 93-120 as dependent thereon.

In view of the foregoing, Applicant submits that the rejections under 35 U.S.C. § 103 have been obviated or overcome and should be withdrawn.

### CONCLUSION

Applicant respectfully requests that the amendment and remarks made herein be entered and made of record in the instant application. If any issues remain in connection herewith, the Examiner is respectfully invited to telephone the undersigned to discuss the same.

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Respectfully submitted,



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